

Tumors with high-density tumor infiltrating lymphocytes constitute a favorable entity in breast cancer: a pooled analysis of four prospective adjuvant trials.

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Abstract

BACKGROUND:

Tumor infiltrating lymphocytes (TILs) are considered in the prognosis of breast cancer (BC) patients. Here, we investigated the prognostic/predictive effect of TILs in patients treated in the frame of four prospective trials with adjuvant anthracycline-based chemotherapy in the pre- and post-trastuzumab era.

METHODS:

TILs density was histologically assessed as percentage of stromal area on whole routine sections of 2613 BC (1563 Luminal A/B; 477 Luminal HER2; 246 HER2-enriched; 327 triple negative [TNBC]) and were evaluated as high/low at three cut-offs (c/o; 50% [lymphocytic predominance, LP], 35% and 25%), in separate training and validation sets.

RESULTS:

High TILs were present in 3.5%, 6.5% and 11.5% of all tumors, using the 50%, 35% and 25% c/o, respectively. TILs status did not interact with BC subtypes or trastuzumab treatment. LPBC patient outcome was not affected by nodal status, while high TILs were favorable in TNBC with unfavorable nodal status. When adjusted for standard clinicopathological parameters and treatment, high TILs independently predicted for favorable outcome, e.g., disease-free survival with the 35% c/o in the entire cohort (HR = 0.44, 95% CI 0.28-0.69, $p < 0.001$) and in specific subtypes.

CONCLUSIONS:

High TILs tumors, especially LPBC seem worthy validating as a separate entity of favorable prognosis in breast cancer.